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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Application Number: 09/868,338
Filing Date: June 18, 2001
Appellant(s): KANNO ET AL.

Shelly Guest Cermak
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed 4/26/05.

***(1) Real Party in Interest***

S.00

A statement identifying the real party in interest is contained in the brief.

***(2) Related Appeals and Interferences***

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

***(3) Status of Claims***

The statement of the status of the claims contained in the brief is correct.

***(4) Status of Amendments After Final***

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

***(5) Summary of Invention***

The summary of invention contained in the brief is correct.

***(6) Issues***

The appellant's statement of the issues in the brief is correct.

***(7) Grouping of Claims***

The rejection of claims 7 and 5-16 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

***(8) Claims Appealed***

The copy of the appealed claims contained in the Appendix to the brief is correct.

***(9) Prior Art of Record***

Christopher F. Higgins, ABC Transporters: From Microorganisms to Man, Annu. Rev. Cell. Biol., Vol. 8, 1992, pp. 67-113

***(10) Grounds of Rejection***

The following ground(s) of rejection are applicable to the appealed claims:

Claims 7 and 15-16 rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. This rejection is set forth in a prior Office Action, mailed on 1/14/2004.

Claims 7 and 15-16 rejected under 35 U.S.C. 112, 1st Paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. This rejection is set forth in a prior Office Action, mailed on 1/14/2004.

**Response To Arguments**

Appellant's arguments are summarized below. Appellant argues:

The asserted utility of the claimed DNA and protein of the present invention is that they are useful for breeding of a microorganism for the purpose of modifying transport of amino acids across a cell membrane. The claimed DNA and protein are argued to be members of a family of DNA/proteins, which are known in the art as ATP binding cassette transporters (ABC transporters). The ATP transporters are argued to have an established physiological function of uptake and excretion of substances into and out of the cell. This has been argued to be an important and defined function in the cell machinery, allowing a cell to excrete toxic and unneeded substances, while

importing useful substances for its metabolism. Transporters are argued to have a defined and credible usefulness which is practical in that these proteins can be expressed in a cell and effect the transport of substances, and in the instant invention, amino acids, inside and outside of the cell. Appellant also argues any person of ordinary skill in the art would recognize this utility as useful in its currently available form and not merely an object of further use testing

Appellant's arguments have been fully considered but are not found persuasive for the reason given below:

Based on the record, there is not a "well established utility" for the claimed ABC transporter because the function, activity and amino acids transported by claimed invention have not been disclosed. The ABC transporters comprise a family of functionally and pharmacologically diverse compound transporters with diverse effects (see Higgins).

Higgins, page 68 and Table 1, discloses that the designation ABC transporters recognize a highly conserved ATP-binding cassette, which is the most characteristic feature of this super family. Some ABC transporters require an associated periplasmic receptor for uptake, others do not. Some ABC transporters have a role in multidrug resistance, others do not. Over 50 ABC transporters were known in 1992. Typically, ABC transporters utilize the energy of ATP hydrolysis to pump substrates across the membrane against a concentration gradient, but again there are exceptions. Each ABC transporter is relatively specific for a given substrate. ABC transporters are specific for amino acids, sugars, inorganic ions, polysaccharides, peptides, and even

proteins have been characterized (Table 1). Some ABC transporters are uptake (import) systems that accumulate substrate within the cell, while others export substrate from the cell, none has been identified that can pump in both directions.

Further, page 78, Higgins discloses, comparison of the amino acid sequences of the transmembrane domains of one transporter with those of another reveals little or no significant similarity (except for a few specific cases). The only significant sequence conservation between the transmembrane domains of several different ABC transporters is a short motif identified on many bacterial transporters. Sequence similarity has been detected between the yeast STE6 peptide transporter and Hlyb hemolysin exporter, and human P-glycoprotein (all transport different compounds)

On page, 86 Higgins discloses, ABC transporters have been identified for almost every class of substrate imaginable, including sugars, peptides, inorganic ions, amino acids, oligopeptides, polysaccharides, and proteins (Table 1). Not only are these substrates chemically very different, but they also vary enormously in size. Higgins discloses the mechanism by which transport diversity is achieved, while each transporter retains a high degree of selectivity for its own particular substrate, it "presents an intriguing problem". On page 88, Higgins discloses, even close similarities between ABC transporters can be misleading. The Mal and Ugp transport systems of *E. coli* are closely related yet handle different substrates and the two human mdr genes are very similar to each other, yet only one is able to mediate drug transport.

The specification does not disclose the compounds transported by the claimed transporter. The prior art discloses that the substrate transported cannot be determined

based solely on sequence homology of the ABC transporter family. It is not even clear if claimed invention is an import or an export system. It is highly unlikely that the claimed transporter has both import and export activities for the same compound since Higgins discloses that no ABC transporters have been identified that can pump in both directions. Does the claimed ABC transporter import or export amino acids, sugars, inorganic ions, polysaccharides, peptides or some other compound? In instant case, will the export or import of a compound be useful for breeding of a microorganism while modifying transport of amino acids across a cell membrane? As pertaining to claimed invention, which amino acid will be imported or exported and be beneficial for microbial breeding? The specification provides no answers to the questions asked above, and only states that import and export of amino acids can be useful in breeding microorganisms. There are no examples provided in the specification or prior art that the claimed ABC transporter of SEQ ID NO:9 has been used to affect the breeding of a microorganism by the modifying the transport of a specific amino acid, or any amino acids, across a cell membrane.

Therefore, the utilities asserted by Appellant are not specific or substantial. Neither the specification nor the art of record disclose the protein of SEQ ID NO:9 encoded by the DNA of SEQ ID NO:7 or fragments thereof useful for the purpose of breeding of a microorganism for the purpose of modifying transport of amino acids across a cell membrane. There is no disclosure of the beneficial affects of claimed transporter in bacteria, which can be utilized for breeding. Thus the corresponding asserted utilities for the claimed ABC transporter, with no disclosed ligands or

compounds which it transports, are essentially methods which do not define a "real world" context of use. It would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a real world context of use for the ABC protein/DNA and fragments thereof, further experimentation is necessary to attribute a utility to the claimed invention. See Brenner v. Manson, 383 U.S. 519, 535B36, 148 USPQ 689, 696 (1966) (noting that Congress intended that no patent be granted on a chemical compound whose sole utility consists of its potential role as an object of use-testing, and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.").

The specification discloses the claimed ABC protein/DNA is related to other proteins of the ABC transporter family. Appellant has used the homology data to form the basis for the utility of the claimed ABC protein/DNA. There is no disclosure in the art that proteins/DNA which have the homology disclosed in the specification are sufficiently similar and have the same function and transport the same compounds. Based on the art and specification it can only be concluded that the ABC transporters comprise a family of functionally and pharmacologically diverse compound transporters, having diverse effects and sharing no one common substrate which can be useful for microbial breeding. Therefore, the first question is, to which family of proteins does the claimed ABC transporter belong? Secondly which particular member of the family of ABC transporters has the same identical activities and functions of the ABC transporter

of SEQ ID NO:9? The specification provides no clear answers. The claimed invention may have its own unique transport properties, in which case it may be the first member of a new class of transporters. Further research is required on the claimed invention to answer the questions raised above. Further, there is no disclosure when a specific species of the ABC transporter family is sufficiently similar to the claimed invention to be considered having the same functionality and activity of that member. There is no disclosure in the specification of the percent identity to related family members of the ABC transporter family that can be used to assign a specific functionality to claimed invention. Appellant has made sequence related predictions based on a limited homology between proteins, and based utility arguments on the family of proteins that have shown the closest identity. Based on the diversity of activity, functionality and ligand specificity of the ABC transporter family further experimentation is required to attach a specific function to the claimed ABC transporter. The specification does not disclose the specific function of the claimed ABC transporter, the transporter mechanism involved in movement of molecules across cell membranes or the amino acids that are moved. The transport mechanism of the claimed invention is not disclosed.

Based on Appellant's arguments the utility for claimed transporter lies in its ability to transport amino acids in and out of a cell. The examiner has argued, based on the art, that all transporters do not transport the same compounds; they are very specific in their substrate specificity. The specific amino acid transported by claimed invention, which is critical to forming the basis for the utility argument, was at the time of filing

unknown. Therefore the claimed invention cannot be used to manipulate a microorganism for the utility of breeding without first experimenting to discover the specific compound transported. There is no disclosure of the scientific reasoning that sequence similarity between other proteins can be used to selectively predict a specific function, dysfunction, and activity of the claimed ABC transporter. The utility of claimed ABC transporter, as argued by appellant, consists of its potential role as an object of use-testing. The claimed ABC protein/DNA, is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, a specific, substantial and credible utility might be found for the claimed polypeptide/DNA. This further characterization, however, is part of the act of invention and until it has been undertaken, Appellant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are useful to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of useful as it appears in 35 U.S.C.101, which requires that an invention must have either an immediately apparent or fully disclosed real world utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the

> public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an appellant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the claimed protein/polynucleotide was, as of the filing date, useful for breeding of a microorganism for the purpose of modifying transport of amino acids across a cell membrane. Even if the compound that is transported by claimed transporter is discovered it is not disclosed how that knowledge will directly relate to breeding microorganisms. Further experimentation is still needed to determine how modification of the transport of that compound will affect microbial growth, if any. Will increase in transport be beneficial? Will decrease in transport be beneficial? What compound will be used to increase or decrease transport? These are further questions, which require addition research. Therefore, until some actual and specific significance can be attributed to the claimed ABC protein/DNA, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or real world utility as of the filing date.

The ABC protein/DNA may share some structural similarity to the ABC transporter family based on undisclosed sequence similarity. The ABC transporter family may have diverse effects. Although the family ABC transporter proteins may share some common structural motifs to claimed ABC protein/DNA, various members of

the family may have different sites of action and different biological effects. In the absence of knowledge of the ligand for claimed invention, molecules transported, or the biological significance of the claimed ABC protein/DNA, there is no immediately evident patentable use. To employ the protein/DNA of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility, which alone, does not support patentability. Since the instant specification does not disclose a credible real world use for claimed polypeptide, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. 101 as being useful. Further there is no disclosure of what is the critical structure of the invention that is required for functionality.

The claimed ABC protein/DNA belongs is a family in which the members have divergent functions based on which tissues the protein is expressed or administered to. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family.

The diversity of the family of proteins, to which claimed ABC transporter is suggested to belong, has already been described. Without some common biological

activity for the family members, a new member would not have a specific, substantial, or credible utility when relying only on the fact that it has structural similarity to the other family members. The members of the family have different biological activities, which may be related to tissue distribution but there is no evidence that the claimed compounds share any one of diverse number of activities. That is, no activity is known to be common to all members. Without knowing a biological significance of the claimed polypeptide/DNA, one of ordinary skill in the art would not know how to use the claimed invention in its currently available form in a credible real world manner based on the diversity of biological activities possessed by the ABC transporter family. Contrast *Brenner*, 148 USPQ at 694 (despite similarity with adjacent homologue, there was insufficient likelihood that the steroid would have similar tumor-inhibiting characteristics), with *In re Folkers*, 145 USPQ 390, 393 (CCPA 1965) (some uses can be immediately inferred from a recital of certain properties) or *In re Brana*, 34 USPQ 1436, 1441 (Fed. Cir. 1995) (evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility; here, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement).

For all the above reasons, the disclosure is insufficient to teach one of skill in the art how to use the invention. For reasons set forth above the disclosure satisfies none of the three criteria *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might

be involved if an appellant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.)

Also, for reasons set forth above, Appellant has not presented sufficient evidence to support specific utility for ABC transporter or its variants.

The rejection under 101 follows *Brenner v. Manson*, as set forth above. In that case, the absence of a demonstrated specific utility for the claimed steroid compound was not ameliorated by the existence of a demonstrated general utility for the class. Unlike *Fujikawa v. Wattanasin*, where there were pharmaceutically acceptable in vitro results, here, there is nothing other than relatively low levels of sequence homology to a broad and diverse family of proteins having distinct modes of activity, and no disclosed common mode of action. A rejection under 112, first paragraph, may be affirmed on the same basis as a lack of utility rejection under 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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June 29, 2005

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